Randomized controlled trials on the comparative effect of treatment modalities of central sleep apnea with Cheyne–Stokes Respiration on cardiovascular outcomes and physiology studies required

Schwarz, Esther I ; Kohler, Malcolm

DOI: https://doi.org/10.5664/jcsm.8306

https://doi.org/10.5664/jcsm.8306

JCSM | Journal of Clinical Sleep Medicine

LETTERS TO THE EDITOR

Randomized controlled trials on the comparative effect of treatment modalities of central sleep apnea with Cheyne–Stokes Respiration on cardiovascular outcomes and physiology studies required

Response to Hunasikatti M. Effect of treatment of central sleep apnea/Cheyne-Stokes Respiration on left ventricular ejection fraction in heart failure: a network meta-analysis is not the answer. *J Clin Sleep Med*. 2020;16(4):651–652. doi:10.5664/jcsm.8304

Esther I. Schwarz, MD[1,2]; Malcolm Kohler, MD[1,2]

[1]*Department of Pulmonology and Sleep Disorders Centre, University Hospital Zurich, Zurich, Switzerland;* [2]*Centre of Competence Sleep & Health Zurich, University of Zurich, Zurich, Switzerland*

We thank Dr. Hunasikatti for his interest in our recently published network meta-analysis on the effects of established treatment modalities for central sleep apnea with Cheyne–Stokes Respiration (CSA/CSR) in heart failure—continuous positive airway pressure (CPAP), adaptive servo-ventilation (ASV), and nocturnal oxygen—on cardiac function.[1,2] We agree that this meta-analysis on cardiac function does not provide an answer to the important question whether and how treating CSA/CSR affects cardiovascular mortality. However, because an impaired cardiac function is the hallmark of heart failure, treatment effects on this outcome are of interest. Small randomized controlled trials, especially on the comparative effectiveness of CPAP and ASV in patients with heart failure and CSA/CSR, have provided contradictory findings. Pooling data from comparable randomized controlled trials helps to estimate treatment effects more precisely and thus come to a more reliable conclusion. In addition, the network approach allows to combine evidence from both direct comparisons of interventions within randomized controlled trials and indirect comparisons across trials based on a common comparator, which is an important aspect because several small studies on 3 different treatment approaches for CSA/CSR (comparing these to an inactive control or to each other) are being used. Therefore, this network meta-analysis currently provides the best evidence on the effects of nocturnal positive pressure ventilation and oxygen supplementation on cardiac function in patients with heart failure and CSA/CSR. In addition, the aim was to analyze the role of patient characteristics (although only possible on a study level), eg, severity of heart failure or CSA/CSR on the treatment effect on cardiac function, to better understand which patient types should be studied in future randomized controlled trials. The analysis led to the conclusion that both CPAP and ASV result in an improvement of left ventricular ejection fraction (LVEF) of about 5%, which is close to the minimum important difference and echocardiographic measurement accuracy in LVEF. The effect size has been discussed in the context of measurement accuracy, minimum important difference, and, in comparison to heart failure treatment with drugs. In addition, we concluded that there are not enough data from randomized controlled trials using supplemental oxygen in these patients. The meta-analysis also demonstrated that within the spectrum of systolic heart failure, the beneficial treatment effect on LVEF was larger in more severe systolic heart failure.[1]

In agreement with Dr Hunasikatti,[2] we discussed that there are several unanswered questions in regard to treatment indications and modalities in patients with CSA/CSR. The underlying mechanisms of the observed increased cardiovascular mortality in the ASV arm of the SERVE-HF trial[3] (Treatment of Sleep-Disordered Breathing with Predominant Central Sleep Apnea by Adaptive Servo Ventilation in Patients with Heart Failure) are still not understood. Therefore, ongoing randomized controlled trials like the Effect of Adaptive Servo-Ventilation on Survival and Cardiovascular Hospital Admissions in Patients with Heart Failure and Sleep Apnea (ADVENT) trial[4] and new trials in both patients with CSA/CSR and heart failure with preserved and with reduced ejection fraction are needed to provide evidence to guide clinical practice. In addition, there is also a need for physiological studies on the effect of positive pressure ventilation on hemodynamics in heart failure. These aspects and current limitations of our understanding of the role of CSA/CSR and its treatment are discussed in the network meta-analysis.[1]

CITATION

Schwarz EI, Kohler M. Randomized controlled trials on the comparative effect of treatment modalities of central sleep apnea with Cheyne–Stokes Respiration on cardiovascular outcomes and physiology studies required. *J Clin Sleep Med*. 2020;16(4):653–654.

REFERENCES

1. Schwarz EI, Scherff F, Haile SR, Steier J, Kohler M. Effect of treatment of central sleep apnea/Cheyne–Stokes Respiration on left ventricular ejection fraction in heart failure: a network meta-analysis. *J Clin Sleep Med*. 2019;15(12):1817–1825.

2. Hunasikatti M. Effect of treatment of central sleep apnea/Cheyne-Stokes respiration on left ventricular ejection fraction in heart failure: a network meta-analysis is not the answer. *J Clin Sleep Med*. 2020;16(4):651–652.
3. Cowie MR, Woehrle H, Wegscheider K, Angermann C, d'Ortho MP, Erdmann E, Levy P, Simonds AK, Somers VK, Zannad F, Teschler H. Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure. *N Engl J Med*. 2015;373(12):1095–1105.
4. Lyons OD, Floras JS, Logan AG, Beanlands R, Cantolla JD, Fitzpatrick M, Fleetham J, John Kimoff R, Leung RS, Lorenzi Filho G, Mayer P, Mielniczuk L, Morrison DL, Ryan CM, Series F, Tomlinson GA, Woo A, Arzt M, Parthasarathy S, Redolfi S, Kasai T, Parati G, Delgado DH, Bradley TD. Design of the effect of adaptive servo-ventilation on survival and cardiovascular hospital admissions in patients with heart failure and sleep apnoea: the ADVENT-HF trial. *Eur J Heart Fail*. 2017;19(4):579–587.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication January 23, 2020
Submitted in final revised form January 23, 2020
Accepted for publication January 23, 2020
Address correspondence to: Esther I. Schwarz, MD, Department of Pulmonology and Sleep Disorders Centre, University Hospital Zurich, Zurich, Switzerland; Email: estherirene.schwarz@usz.ch

DISCLOSURE STATEMENT

The authors report no conflicts of interest.